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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,893	02/12/2004	John Rush	CST-201 CIP	6794

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/777,893	RUSH ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *40-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-48* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/04 & 5/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-39, drawn to a method of isolating a modified peptide from a complex mixture, classified in class 435, subclass 4.

II. Claims 40-43, drawn to an immunoaffinity isolation device comprising a support comprising of one modification-specific antibody immobilized to a rigid, non-porous or macroporous resin, classified in class 436, subclass 531.

III. Claims 44-48, drawn to an antibody, classified in class 424, subclass 130.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the process can be practiced by another materially different apparatus such as a filter or test strip with immobilized antibody.

Inventions III and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the antibody that binds ubiquitin fusion degradation protein 1 (UFD1) only when phosphorylated at serine 335, but does not substantially bind to UFD1 when not phosphorylated at this residue can be used to identify serine 335 and the antibody of claim 45 can be used to identify serine 558.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and they have different modes of operation, different functions because the device has an antibody immobilized on a support can be used as a capture reagent in a solid phase assay while the specific antibody in claims 44-48 can be used to detect phosphorylation at different serines.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II or III, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. James Cullem on March 31, 2005 a provisional election was made with traverse to prosecute the invention of group I, claims 1-39. Affirmation of this election must be made by applicant in replying to this Office action. Claims 40-48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for reciting "modified peptide" because it is unclear how the peptide is modified, i.e. the amino acid sequence is altered? Or the mass of the peptide is altered?

Claim 7 is vague. It is unclear if the enzyme is immobilized to the same solid support in claim 1 that has the immobilized antibody or to something else.

Claim 3, 18, 30, 32 and 36 recites abbreviations, i.e. MALDI-TOF MS, LC-MS3; MAPK, PKA, PKC etc. Please spell out the abbreviations for abbreviations may have more than one word.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-29 of copending Application No. 10/175,486. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the

United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 9-12, 19, 20, 22-24, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Little et al. (US 6,322,970).

Little teaches a method for isolating a modified peptide from a complex mixture of peptides; said method comprising the steps of :

a) obtaining a proteinaceous preparation from an organism wherein the proteinaceous preparation comprises the peptides from two or more different proteins;

b) contacting said proteinaceous preparation with at least one immobilized modification-specific antibody; and (see col. 21, lines 25-27).

c) isolating at least one modified-peptide specifically bound to said immobilized modification specific antibody in step (b)

A target polypeptide is isolated prior to being detected by mass spectrometric analysis (equivalent to claim 2 of the present invention). For examples, the target polypeptide can isolated from a cell or tissue obtained from a subject such as a human. The target polypeptide can be isolated using a reagent that interacts specifically with the target polypeptide, for example, an antibody that interacts specifically with the target polypeptide, or the target polypeptide can be fused to a tag peptide and isolated using an antibody that interacts specifically with the tag peptide. The target polypeptide can be immobilized to a solid support such as a bead or a microchip which can be a flat surface. (see col. 4, lines 24-45). The polypeptide means at least two amino acids, or amino acid derivatives, including mass modified amino acids, that are linked by a peptide bond, which can be a modified peptide bond. The polypeptide can be

chemically synthesized and can be modified by chemical or enzymatic methods following translation or chemical synthesis (see col. 9, lines 30-45). The proteinaceous preparation from an organism is equivalent to a biological sample obtained from a living source, an animal, a plant, or solid material such as a tissue, cells, a cell extract, or biological fluid such as urine, blood, saliva, amniotic fluid etc. (see col. 9, lines 21-30). The target polypeptide can be isolated by affinity purification using an antibody, avidin or other specific reagent covalently linked to a solid support. In such a method, the translation reaction is poured over the support, and the polypeptide is bound due to its specificity interacting with the reagent. Regarding claims 9, Little teaches that target polypeptide fused to a tag peptide can be isolated on a column or bed of chelated zinc or copper ions. Beds or columns having such divalent metal ions chelated thereto can be obtained from commercial source or prepared by using methods known in the art. It is thus inherent that the antibody is immobilized in chromatography resin within a column (see col. 21, lines 25-39). Regarding claim 3, Little teaches that the mass spectrometry comprises MALDI-TOF (see col. 54, lines 46-60; col. 55, lines 29-35). The modification-specific antibody is a monoclonal or a polyclonal antibody (see col. 20, lines 20-54). The identification of the target polypeptide indicates a marker of a disease (see col. 57, lines 49-52).The molecular mass of the a target polypeptide is determined by mass spectrometry and is compared to a standard, whereby the identity of the polypeptide can be ascertained. (see col. 3, lines 15-20). Regarding claim 22, Little teaches that "determining the identity of a target polypeptide" refers to determining at least one characteristic of the polypeptide, for example, a molecular mass or charge, or

the identity of at least one amino acid, or identifying a particular pattern of peptide fragments of the target polypeptide and comparing such characteristic with a polypeptide in a reference sample. (see col. 9, lines 45-55; col. 10, lines 16-55). The proteinaceous preparation corresponds to a diseased organism and the reference sample corresponds to a normal organism (see example 1). The disease is cancer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. (US 6,322,970) in view of Pidgeon et al. (US 6,579,720).

Little has been discussed above.

However, Little fails to teach that the column being coupled to a mass spectrometer.

Pidgeon teaches a method of analyzing a compound using High Performance Liquid Chromatography (HPLC) coupled with a mass spectrometer to produce at least two sets of eluent fractions. (see col. 6, line 65-col. 7, line 41).

Since Little teaches that the target polypeptide can be isolated on a chromatography column and using mass spectrometry to analyze the polypeptide, it would have been obvious to one of ordinary skills in the art to use the HPLC column coupled to a mass spectrometer taught by Pidgeon in the method of Little because with

the mass spectrometer coupled to the column, the eluents or the polypeptides can be readily analyzed without being transported to the mass spectrometer if the column were not coupled to the mass spectrometer. Thus, analysis or the spectral profiles of the targets can be quickly and conveniently obtained.

Claims 13-16, 30, 32, 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. (US 6,322,970) in view of Goshe et al. (US 6,818,454).

Little has been discussed above.

However, Little fails to teach that the modification comprises phosphorylation; said modified peptide is a phosphopeptide; said modification-specific antibody comprises a motif-specific, context-independent antibody that recognizes a motif comprising at least one phosphorylated amino acid; and said motif consists of a single phosphorylated amino acid. Little also fails to teach fractionating phosphopeptides by reversed-phased-chromatography and a motif specific, context-independent antibody comprises a general phosphotyrosine-specific antibody, a general phosphothreonine-specific-antibody or a general phosphoserine-specific antibody.

Goshe teaches a method for identifying a phosphorylation states of proteins. Proteins may be modified to contain phosphate groups at either some or all of their serine, threonine, tyrosine, histidine and/or lysine amino acid residues. The method applies to peptides that generated via enzymatic or chemical processing. The method is followed by protein sequencing via tandem mass spectrometry, chromatography separation (see col. 2, line 26-col. 3, line 60). In the method, the enriched mixture of

biotinylated phosphopeptides was analyzed by capillary reversed-phase liquid chromatography followed by mass spectrometry (MS). (see col. 16, lines 48-53).

It would have been obvious to one of ordinary skills in the art to fractionate the phosphopeptides using reversed-phase chromatography followed by mass spectrometry suggested by Goshe in combination with the method of isolating a modified peptide using a capture antibody taught by Little since both teach a method of isolating peptides using a mass spectrometer. To date several disease states have been linked to the abnormal phosphorylation/dephosphorylation of specific proteins. Thus, it would be an advantage to combine the two methods of Little and Goshe to study the phosphorylated peptides which might link to several disease states such as Alzheimer's disease, cancer which might further lead to the development of improved diagnostics for the detection of various diseases. (see Goshe, col. 2, lines 2-25). It would have been obvious to one of ordinary skills in the art to generate specific antibody comprising a motif-specific, context-independent antibody that recognizes a motif of at least one phosphorylated amino acid; and said motif consists of a single phosphorylated amino acid such as serine, threonine, tyrosine and histidine using the combined method of Goshe and Little since these amino acids contain phosphate group and contribute to phosphorylation. Abnormal phosphorylation of specific proteins link to several disease states. Studying these disease states would lead to the development of improve diagnostics for the detection of various diseases.

Allowable Subject Matter

Claims 4-8, 17, 18, 21, 25, 26, 28, 29, 31, 33, 35-39 are free of prior arts.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
April 27, 2005

Christopher L. Chin

CHRISTOPHER L. CHIN
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GROUP ~~1800~~ 1641
5/4/05